

**IN THE CLAIMS:**

Please amend the following claims:

82. A method of screening a sample of body fluid for at least one autoantibody to at least one antigen, which method comprises:

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- (a) providing a source of said at least one antigen to said autoantibody;
  - (b) providing a substrate having immobilized thereto at least one antibody to said antigen of step (a);
  - (c) contacting said antigen source of step (a) with said sample of body fluid, so as to obtain a mixture wherein said antigen is allowed to bind with said autoantibody, when the latter is present in said sample;
  - (d) allowing said mixture obtained in step (c) to flow along said substrate of step (b) and to interact with said antibody immobilized to said substrate;
  - (e) providing labeling means so as to permit monitoring of binding of said autoantibody and said antigen present in said mixture obtained in step (c); and
  - (f) monitoring said binding so as to provide an indication of the presence of said autoantibody in said sample of body fluid.

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87. A method according to claim 82, which comprises contacting in step (c) said antigen source and said sample of body fluid with at least one non-immobilized antibody to said antigen.

88. A method according to claim 87, wherein said non-immobilized antibody is provided in purified form.

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94. A method according to claim 93, wherein at least said sample of body fluid is contacted with an application zone of said substrate, which application zone is provided upstream of said immobilized antibody on said substrate and wherein said mixture is allowed to flow from said application zone along said substrate so as

B<sub>8</sub> cont to interact with said immobilized antibody.

96. A method according to claim 94, wherein said application zone further includes at least one non-immobilized antibody to said antigen, and said mixture in step (c) is obtained by contacting said sample of body fluid and said antigen with said non-immobilized antibody present in said application zone.

B<sub>9</sub> 97. A method according to claim 94, wherein said antigen source of step (a) and said sample of body fluid are contacted remote from said substrate so as to provide said mixture of step (c), and said mixture is subsequently contacted with said application zone.

98. A method according to claim 97, wherein said antigen source of step (a), said sample of body fluid and at least one non-immobilized antibody to said antigen, are contacted remote from said substrate so as to provide said mixture of step (c), and said mixture is subsequently contacted with said application zone.

B<sub>10</sub> 100. A method according to claim 82, wherein said immobilized antibody is in purified form.

104. A method according to claim 103, wherein said antigen includes a binding site to which either said autoantibody or said immobilized antibody can bind, whereby in step (d) binding of said immobilized antibody to said binding site is precluded where said autoantibody has bound to said binding site in step (c).

B<sub>11</sub> 105. A method according to claim 82, which comprises screening said sample of body fluid for at least a first and a second autoantibody to said antigen, wherein at least first and second antibodies to said antigen are immobilized on said substrate in step (b).

106. A method according to claim 105, wherein said antigen includes:  
a first binding site to which either said first autoantibody or said first immobilized antibody can bind, whereby in step (d) binding of said first immobilized

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antibody to said first binding site is precluded where said first autoantibody has bound to said first binding site in step (c); and

a second binding site to which either said second autoantibody or said second immobilized antibody can bind, whereby in step (d) binding of said second immobilized antibody to said second binding site is precluded where said second autoantibody has bound to said second binding site in step (c);

wherein said first and second binding sites are distinct sites on said antigen.

109. A method according to claim 87, wherein said non-immobilized antibody is provided with said labeling means, which non-immobilized antibody is capable of binding to a site on said antigen distinct from a binding site for either (i) said autoantibody or autoantibodies being screened or (ii) said immobilized antibody, whereby in step (d), antigen is allowed to be bound both to said immobilized antibody and to said non-immobilized antibody.

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110. A method according to claim 87, which comprises screening said sample of body fluid for at least first and second autoantibodies to said antigen, wherein said non-immobilized antibody is capable of binding to a site on said antigen to which either said first or second autoantibody can bind and which is distinct to a binding site on said antigen for said immobilized antibody, whereby in step (d) antigen is allowed to be bound both to said immobilized antibody and to said non-immobilized antibody.

111. A method according to claim 110, wherein said antigen includes:  
a first binding site to which either said first autoantibody or said immobilized antibody can bind, whereby in step (d) binding of immobilized antibody to said first binding site is precluded where said first autoantibody has bound to said first binding site in step (c); and

a second binding site to which either said second autoantibody or said non-immobilized antibody can bind;

wherein said first and second binding sites are distinct sites on said antigen.

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114. A method according to claim 87 which further comprises a positive

control that is present in the presence or absence of the autoantibody or autoantibodies being screened, wherein the positive control comprises attaching to the substrate at least one control agent that can bind to the at least one non-immobilized antibody.

115. A kit for use in screening a sample of body fluid for at least one autoantibody to at least one antigen, which kit comprises:

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- (a) a source of said at least one antigen to said autoantibody;
  - (b) a substrate having immobilized thereto at least one antibody to said antigen;
  - (c) means for contacting said antigen source with said sample of body fluid, so as to obtain a mixture wherein said antigen is allowed to bind with said autoantibody, when the latter is present in said sample;
  - (d) means for allowing said mixture to flow along said substrate and to interact with said antibody immobilized to said substrate;
  - (e) labeling means to permit monitoring of binding of said autoantibody and said antigen present in said mixture; and
  - (f) means for monitoring said binding so as to provide an indication of the presence of said autoantibody in said sample of body fluid.

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120. A kit according to claim 115, which further comprises a source of at least one non-immobilized antibody to said antigen and means whereby said non-immobilized antibody can be contacted with said antigen source and said sample of body fluid.

121. A kit according to claim 120, wherein said non-immobilized antibody is provided in purified form.

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126. A kit according to claim 115, wherein said substrate comprises an application zone for at least said sample of body fluid, which application zone is provided upstream of said immobilized antibody on said substrate, whereby said mixture is allowed to flow from said application zone along said substrate so as to interact with said immobilized antibody.

128. A kit according to claim 126, wherein said application zone further includes at least one non-immobilized antibody to said antigen, and means whereby said mixture is obtained by contacting said sample of body fluid and said antigen with said non-immobilized antibody present in said application zone.

B<sub>16</sub> 129. A kit according to claim 126, wherein means are provided whereby said antigen source and said sample of body fluid are contacted remote from said substrate so as to provide said mixture and means whereby said mixture is subsequently contacted with said application zone.

130. A kit according to claim 129, wherein means are provided whereby said antigen source, said sample of body fluid and at least one non-immobilized antibody to said antigen, are contacted remote from said substrate so as to provide said mixture, and means whereby said mixture is subsequently contacted with said application zone.

B<sub>17</sub> 132. A kit according to claim 115, wherein said immobilized antibody is provided in purified form.

B<sub>18</sub> 135. A kit according to claim 115, for screening said sample of body fluid for one said autoantibody, wherein said antigen includes a binding site to which either said autoantibody or said immobilized antibody can bind, whereby binding of said immobilized antibody to said binding site is precluded where said autoantibody has previously bound to said binding site.

B<sub>19</sub> 137. A kit according to claim 136, wherein said antigen includes:  
a first binding site to which either said first autoantibody or said first immobilized antibody can bind, whereby binding of said first immobilized antibody to said first binding site is precluded where said first autoantibody has previously bound to said first binding site; and

a second binding site to which either said second autoantibody or said second immobilized antibody can bind, whereby binding of said second immobilized

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cont antibody to said second binding site is precluded where said second autoantibody has previously bound to said second binding site;

wherein said first and second binding sites are distinct sites on the antigen.

140. A kit according to claim 120, wherein said non-immobilized antibody is provided with said labeling means, which non-immobilized antibody is capable of binding to a site on said antigen distinct from a binding site for either (i) said autoantibody or autoantibodies being screened or (ii) said immobilized antibody, whereby antigen is allowed to be bound both to said immobilized antibody and to said non-immobilized antibody.

B<sub>20</sub> 141. A kit according to claim 120 for screening said sample of body fluid for at least first and second autoantibodies to said antigen, wherein said non-immobilized antibody is capable of binding to a site on said antigen to which either said first or second autoantibody can bind and which is distinct to a binding site on said antigen for said immobilized antibody, whereby antigen can be bound both to said immobilized antibody and to said non-immobilized antibody.

142. A kit according to claim 141, wherein said antigen includes:

a first binding site to which either said first autoantibody or said immobilized antibody can bind, whereby binding of immobilized antibody to said first binding site is precluded where said first autoantibody has previously bound to said first binding site; and

a second binding site to which either said second autoantibody or said non-immobilized antibody can bind;

wherein said first and second binding sites are distinct sites on said antigen.

B<sub>21</sub> 145. A kit according to claim 120 which further comprises a positive control that is present in the presence or absence of the at least one autoantibody being screened, wherein the positive control comprises at least one control agent attached to the substrate that can bind to the at least one non-immobilized antibody.

146. A method of screening a patient for at least one autoantibody to at

least one antigen, which method comprises:

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- (a) obtaining a sample of body fluid from said patient;
  - (b) contacting said sample of body fluid of step (a) with an antigen source of a kit according to claim 115, so as to obtain a mixture wherein said antigen is allowed to bind with said autoantibody, when the latter is present in said sample;
  - (c) allowing said mixture to flow along a substrate of said kit and to interact with said antibody immobilized to said substrate; and
  - (d) monitoring binding of said autoantibody and said antigen present in said mixture, so as to provide an indication of the presence of said autoantibody in said sample of body fluid from said patient.
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